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54623 KIRKPATRIO	7590 08/22/200 CK & LOCKHART PRI	o7 ESTON GATES ELLIS LLP	EXAM	IINER	
(FORMERLY KIRKPATRICK&LOCKHART NICHOLSON GRAHAM)			DUFFY, BRADLEY		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)			
	10/770,726	BROWN ET AL.			
Office Action Summary	Examiner	Art Unit			
	Brad Duffy	1643			
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address			
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA  - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication.  - If NO period for reply is specified above, the maximum statutory period w  - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION  16(a). In no event, however, may a reply be time  11 apply and will expire SIX (6) MONTHS from cause the application to become ABANDONE	L. rely filed the mailing date of this communication.			
Status					
1)⊠ Responsive to communication(s) filed on 21 M     2a)⊠ This action is <b>FINAL</b> . 2b)□ This     3)□ Since this application is in condition for allowar closed in accordance with the practice under E	action is non-final. ace except for formal matters, pro				
Disposition of Claims					
4) Claim(s) 1.5-7 and 26-30 is/are pending in the  4a) Of the above claim(s) is/are withdray  5) Claim(s) is/are allowed.  6) Claim(s) 1.5-7 and 26-30 is/are rejected.  7) Claim(s) is/are objected to.  8) Claim(s) are subject to restriction and/or  Application Papers  9) The specification is objected to by the Examined  10) The drawing(s) filed on is/are: a) access applicant may not request that any objection to the of Replacement drawing sheet(s) including the correction  11) The oath or declaration is objected to by the Examined Replacement drawing sheet(s) including the correction in the objected to by the Examined Replacement drawing sheet(s) including the correction in the objected to by the Examined Replacement drawing sheet(s) including the correction in the objected to by the Examined Replacement drawing sheet(s) including the correction in the objected to by the Examined Replacement drawing sheet(s) including the correction in the objected to by the Examined Replacement drawing sheet(s) including the correction in the objected to by the Examined Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected to be the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected Replacement drawing sheet(s) including the correction in the objected sheet and the objected drawing sheet and the objected drawing sheet and the objected draw	on from consideration.  The election requirement.  The epted or b) □ objected to by the Edrawing(s) be held in abeyance. See on is required if the drawing(s) is objected to by the electron is required if the drawing(s) is objected to by the electron is required if the drawing(s) is objected to by the electron is required if the drawing(s) is objected to by the electron is required if the drawing(s) is objected to by the electron is required if the drawing(s) is objected to by the electron is required if the drawing(s) is objected to by the electron is required in the drawing(s) is objected to by the electron is required in the drawing(s) is objected to by the electron is required in the drawing(s) is objected to by the electron is required in the	e 37 CFR 1.85(a). ected to. See 37 CFR 1.121(d).			
Priority under 35 U.S.C. § 119					
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  a) All b) Some * c) None of:  1. Certified copies of the priority documents have been received.  2. Certified copies of the priority documents have been received in Application No  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  * See the attached detailed Office action for a list of the certified copies not received.					
Attachment(s)  1) Notice of References Cited (PTO-892)  2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  3) Information Disclosure Statement(s) (PTO/SB/08)  Paper No(s)/Mail Date	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other: Exhibit, A, B,	te atent Application			

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#### **DETAILED ACTION**

1. The amendment filed May 21, 2007, is acknowledged and has been entered. Claims 21-25 have been cancelled. Claims 1, 5-7 have been amended. Claims 26-30 have been newly added.

- 2. Claims 1, 5-7 and 26-30 are pending in the application and are under examination.
- 3. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

#### **Priority**

4. Applicant's claim under 35 USC §§ 119 and/or 120 for benefit of the earlier filing date of the 60/444,637, filed February 4, 2003, is acknowledged.

However, claims 1, 5-7 and 26-29 do not properly benefit under 35 U.S.C. §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under 35 USC §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

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Accordingly, the effective filing date of claims 1, 5-7 and 26-29<sup>1</sup> is deemed the filing date of the instant application, namely February 4, 2004.

#### Grounds of Objection and Rejection Withdrawn

5. Unless specifically reiterated below, Applicant's amendment and/or arguments filed May 21, 2007, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed February 20, 2007.

#### Grounds of Objection Maintained

6. The objection to the specification because the use of improperly demarcated trademarks is maintained. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Although it appears that Applicant has made a *bona fide* attempt to resolve this issue by appropriately amending the specification, an additional example of an improperly demarcated trademark appearing in the specification is noted, namely Taxol™; see, e.g., paragraph [0101] of the published application.

Again, appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., TM, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <a href="http://www.uspto.gov/web/menu/search.html">http://www.uspto.gov/web/menu/search.html</a>.

#### **Grounds of Rejection Maintained**

<sup>1</sup> Note: Claim 30 is indefinite, as noted below, and cannot be examined for compliance with the requirements set forth under 35 U.S.C. §§ 112, first paragraph, 102, and 103.

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#### Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The rejection of claims 1, 5-7 and 26-29 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a method of detecting colon adenocarcinoma markers comprising detecting an expression profile of at least one nucleic acid in a colon cancer tissue from a human subject, wherein said at least one nucleic acid is selected from the group of SEQ ID NO:26, SEQ ID NO:1, and SEQ ID NO: 12. wherein said at least one nucleic acid is overexpressed compared to a normal colon tissue reference control, and while being enabling for using a method of detecting lung adenocarcinoma markers comprising detecting an expression profile of at least one nucleic acid in a lung cancer tissue from a human subject, wherein said at least one nucleic acid is selected from the group of SEQ ID NO:26, SEQ ID NO:1, and SEQ ID NO: 12, wherein said at least one nucleic acid is overexpressed compared to a normal lung tissue reference control, and while being enabling for using any process encompassed by the claims, which has been described by the prior art, does not reasonably provide enablement for using the claimed processes, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

At page 8 of the amendment filed May 21, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments traversing the ground of rejection set forth in the preceding Office action have been carefully considered but not found persuasive to obviate this rejection.

M.P.E.P. § 2164.01 states:

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which

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postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

The present claims are directed to methods of detecting an expression profile of at least one nucleic acid in a colon or lung cancer tissue from a human subject, wherein said at least one nucleic acid comprises a sequence is selected from the group consisting of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26; comparing said expression profile to a normal tissue reference expression profile of said at least one nucleic acid; and determining whether the nucleic acid is overexpressed compared to the normal tissue reference expression profile, thereby to detect a marker of the colon or lung cancer.

Notably, while Applicant's response at page 8 filed May 21, 2007, does provide evidence that the specification also teaches the overexpression of each of the mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 in lung

cancer tissue, as compared to a normal lung tissue reference expression profile, as well as the overexpression of each of the mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 in colon cancer tissue, as compared to a colon tissue reference expression profile (see page 8, 2<sup>nd</sup> paragraph of the response filed May 21, 2007 and Table 6A of the specification), it is noted that the claims are not limited to comparing the claimed cancer tissue expression profile to a corresponding normal lung or colon tissue profile, respectively; accordingly, the claims are directed to comparing the colon or lung cancer expression profile to any normal tissue reference profile and one of skill in the art would be subject to undue experimentation to use methods of detecting a colon or lung cancer marker, wherein the expression profile of the mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 in a colon cancer tissue or a lung cancer tissue are not compared to a corresponding normal colon tissue reference profile or a corresponding normal lung tissue reference profile, respectively.

Notably, the specification discloses the following about the cancer markers of the invention:

The present invention pertains to the use of the CPKGs listed in Table 1, the transcribed polynucleotides (CPKPN), and the encoded polypeptides (CPKPP) as markers for cancer. Moreover, the use of expression profiles of these genes can indicate the presence of a risk of cancer. (see page 31).

The present invention provides compositions and methods for the diagnosis, prevention, or treatment of numerous cancers. The present invention also provides methods for the identification of novel therapeutic agents for treating cancers. In addition, the present invention provides animal models useful for studying the pathogenesis of cancers. The present invention is based on the discovery of cancer genes that are overexpressed in at least two types of cancer tissues as compared to corresponding cancer-free tissues. In many embodiments, the cancer genes are overexpressed in colon cancer, lung cancer, breast cancer, or prostate cancer tissues, as compared to the corresponding cancer-free tissues. (see page 9).

Thus, for example, while the specification enables the skilled artisan to use processes to detect overexpressed mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 as colon cancer markers by comparing a colon cancer expression profile of the mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 with a expression profile of said mRNAs in a corresponding cancer-free colon tissue, it does not reasonably enable the use of the claimed processes to detect colon or lung cancer markers in which the comparison made is to any "normal tissue reference expression profile", but not necessarily those of normal (i.e., non-cancerous) colon and lung tissues, respectively, because the specification does not teach other normal tissue expression reference profiles that could be used to detect the claimed mRNAs as a "marker" of colon cancer. Furthermore, it is submitted that the skilled artisan cannot predict whether any such comparison to a "normal tissue reference expression profile", where the tissue is not colon or lung tissue, will identify a marker of colon or lung cancer, but in most cases it is expected that it would not.

Thus, contrary to Applicant's argument, the amendment to claim 1 has not obviated the ground of rejection set forth in the preceding Office action because the amendment does not require that the expression profile of the colon cancer tissue be compared to a normal colon tissue reference expression profile as set forth in the preceding Office action. Similarly, while Applicant has provided evidence that the specification would enable detecting the expression profile of mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 in a lung cancer tissue and comparing said expression profile to a normal lung tissue reference expression profile to detect lung cancer markers as the mRNAs comprising the sequence of SEQ ID NO: 1, SEQ ID NO:12, and SEQ ID NO:26 are also overexpressed in lung cancer, the amendment to claim 1 has not enabled using these lung cancer markers as the lung cancer tissue expression profile can be compared to any normal tissue expression profile and one of skill in the art would be subject to undue experimentation to use such methods.

In conclusion, upon careful consideration of the factors used to determine

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whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

#### **New Grounds of Objection**

9. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

In this case, the method of claim 1 is practiced by detecting an expression profile of at least one nucleic acid in a colon cancer tissue, as opposed to a lung cancer tissue, from a human subject having lung cancer in accordance with claim 7, it is unclear how, or whether the limitation recited in claim 7 further limits the subject matter of claim 1.

Must the subject have both colon and lung cancers?

10. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

In this case, the method of claim 1 is practiced by detecting an expression profile of at least one nucleic acid in a colon cancer tissue, as opposed to a lung cancer tissue, from a human subject having lung cancer in accordance with claim 26, it is unclear how, or whether the limitation recited in claim 26 further limits the subject matter of claim 1.

Must the subject have both colon and lung cancers?

#### **New Grounds of Rejection**

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#### Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is indefinite in the recitation of "wherein the sequence is SEQ ID NO:31". This limitation lacks antecedent basis, as claim 1 only refers to "a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:26".

Accordingly, the claim fails to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

#### Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- 14. Claims 1, 7, 26 and 29 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 03/025138 A2 (Afar et al, published March 2003).

The claims are herein drawn to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:26 in a colon cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:26 from normal colon tissue to determine whether

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said nucleic acid is overexpressed in the cancer tissue or to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:26 in a lung cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:26 from normal lung tissue to determine whether said nucleic acid is overexpressed in the cancer tissue.

Afar et al teach methods of detecting an expression profile of an mRNA comprising a nucleotide sequence that is 100% identical to the instantly claimed SEQ ID NO:26 in colon cancer tissues<sup>2</sup>, and comparing said expression profile to the expression profile of an mRNA from corresponding normal colon tissue to determine whether said nucleic acid is overexpressed in the cancer tissue. Afar et al also teach methods of detecting an expression profile of an mRNA comprising a nucleotide sequence that is 100% identical to the instantly claimed SEQ ID NO:26 in lung cancer tissues, and comparing said expression profile to the expression profile of an mRNA from corresponding normal lung tissue to determine whether said nucleic acid is overexpressed in the cancer tissue; see entire document (e.g., SEQ ID NO:27; page 6, lines 4-27; page 23, line 13 through page 25, line 24; page 37, line 26 through page 38, line 12; and page 52, line 16 through page 53, line 32).

Thus, Afar et al anticipate these claims.

#### Claim Rejections - 35 USC § 103

- 15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
  - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

<sup>&</sup>lt;sup>2</sup> See the alignment of these sequences attached here as Exhibit A.

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The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
- 16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
- 17. Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being anticipated by WO 03/025138 A2 (Afar et al, published 2003).

Claims 1, 5, and 6 are directed to the method of claim 1, wherein the normal tissue reference profile is an average expression profile of said at least one nucleic acid in a plurality of reference biological samples of cancer-free subjects and wherein said expression profiles are determined using RT-PCR or nucleic acid arrays.

Additionally, Afar et al teach said expression profiles being determined using RT-PCR or nucleic acid arrays (e.g., page 53, line 6-13).

With regard to claims 5 and 6, it is noted that Afar et al do not expressly teach that the normal tissue reference profile is an "average" expression profile of said nucleic acid from cancer-free subjects. Nevertheless, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to measure the

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expression profile of said at least one nucleic acid in more than one reference biological sample, and then determine the average value of the expression profiles of that nucleic acid in the samples, so as to compare the expression profile of the nucleic acid in the colon cancer tissue and the average value in cancer-free colon tissue or to compare the expression profile of the nucleic acid in the lung cancer tissue and the average value in cancer-free lung tissue, because it would be recognized that the average value better reflects the standard level of expression in normal, non-cancerous colon or lung tissues. This is because it would be expected that the normal level of expression of any nucleic acid will vary in normal subjects, at least to some extent, such that the difference in the levels of expression in the colon or lung cancer tissue and any one specimen of the corresponding normal tissue might be more or less significant, which could lead the practitioner of the process to falsely conclude that the nucleic acid is or is not overexpressed in the cancerous tissue. Therefore, one ordinarily skilled in the art at the time the invention was made to would have been motivated to do so in order to more accurately determine whether or not the nucleic acid is overexpressed in the colon or lung cancer tissue, relative to the standard level of expression that occurs in the corresponding normal tissues.

Because Afar et al. teaches the expression profiles are determined using RT-PCR or nucleic acid array, it would have been *prima facie* obvious to determine the average value of the expression profiles of that nucleic acid in the samples using such methodology. One ordinarily skilled in the art would have been motivated to do so because such methodology was both routine and conventional at the time the invention was made, and was recognized to be very sensitive.

18. Claims 1, 5-7, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,632,936 (Carr, published 2003), in view of US Patent 7,101,985 (Elledge et al, published 2006) and US Patent 6,709,832 (Von Knebel Doebertiz et al, published 2004).

The claims are herein drawn to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:1 in a colon cancer tissue from a human

subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:1 from normal colon tissue to determine whether said nucleic acid is overexpressed in the cancer tissue or to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:1 in a lung cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:1 from normal lung tissue to determine whether said nucleic acid is overexpressed in the cancer tissue. Claims 5 and 6 are further drawn to the method of claim 1, wherein the normal tissue reference profile is an average expression profile of said at least one nucleic acid in a plurality of reference biological samples of cancer-free subjects and wherein said expression profiles are determined using RT-PCR or nucleic acid arrays.

Carr teaches methods of detecting an expression profile of an mRNA that encodes a cell-cycle checkpoint polypeptide comprising SEQ ID NO:1 from lung cancer tissues that is 99.7% identical<sup>3</sup> to the instantly claimed SEQ ID NO:1. Carr also teaches methods of detecting an expression profile of an mRNA that encodes a cell-cycle checkpoint polypeptide comprising SEQ ID NO:1 from colon cancer tissues that is 99.7% identical to the instantly claimed SEQ ID NO:1; see entire document (e.g., column 5, lines 11-33). Carr also teaches said expression profiles being determined using RT-PCR or nucleic acid arrays (e.g., column 5, lines 17-25).

Carr does not expressly teach an mRNA that is 100% identical to the instantly claimed nucleic acid comprising the sequence set forth as SEQ ID NO: 1, nor does Carr expressly teach comparing the expression profile of the mRNA from the colon or lung cancer tissue to the expression profile of the mRNA from corresponding normal colon or lung tissue, respectively, to determine whether said nucleic acid is overexpressed in the cancer tissue.

These deficiencies are made up for in the teachings of Elledge et al and Von Knebel Doebertiz et al.

Elledge et al teach an mRNA comprising a nucleotide sequence (i.e., SEQ ID

<sup>&</sup>lt;sup>3</sup> See the alignment of these sequences attached here as Exhibit B.

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NO: 38), which encodes the **same** cell-cycle polypeptide as the polypeptide referred to by Carr, which is encoded by the disclosed nucleic acid molecule comprising SEQ ID NO: 1. Moreover, the nucleotide sequence of SEQ IID NO: 38, which is disclosed by Elledge et al., is 100% identical<sup>4</sup> to SEQ ID NO: 1; see entire document (e.g., column 53, line 61 to column 54, line 16).

Von Knebel Doebertiz et al teach that it is an obvious thing to compare an mRNA expression profile from a cancerous body sample with a corresponding mRNA expression profile from a body sample which originates from a healthy person) (see entire document, e.g., column 2 lines 45-48 and 59-60).

Therefore, because it would be recognized that both the nucleic acid molecules disclosed by the prior art (i.e., the nucleic acid disclosed by Carr and the nucleic acid disclosed by Elledge et al.) encode the same protein, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to practice the process disclosed by Carr by detecting the expression profile of the nucleic acid disclosed by Elledge et al in both lung cancer tissue and colon cancer tissue. Furthermore, because Von Knebel Doebertiz et al teach that it is an obvious thing to compare an mRNA expression profile from a cancerous body sample with a corresponding mRNA expression profile from a body sample which originates from a healthy person, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to compare said colon cancer expression profile to the expression profile of the same nucleic acid in normal colon tissue or to compare said lung cancer expression profile to the expression profile of the same nucleic acid in normal lung tissue, to determine whether the nucleic acid encoding the protein is overexpressed in the cancer tissue.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to detect expression profiles of the mRNA comprising SEQ ID NO:38 of Elledge as it encodes the same cell-cycle checkpoint polypeptide of Carr. Notably, the polynucleotide sequence

<sup>&</sup>lt;sup>4</sup> See the alignment of these sequences attached here as Exhibit C.

of SEQ ID NO:38 of Elledge adds an additional 26 nucleotides to the 5' untranslated region of the mRNA taught by Carr and therefore, one of skill in the art would have been motivated to detect the mRNA of Elledge as one of ordinary skill in the art would have recognized it to be a more complete mRNA than the mRNA of Carr. Furthermore, one of ordinary skill in the art would have been motivated to compare the expression profile of the mRNA comprising SEQ ID NO:38 from the colon cancer tissue to its expression profile in corresponding normal colon tissue or to compare the expression profile of the mRNA comprising SEQ ID NO:38 from the lung cancer tissue to its expression profile in corresponding normal lung tissue as Von Knebel Doebertiz et al teach that it is obvious to compare a tissue suspected of being cancerous with a corresponding normal tissue, in order to detect cancer markers overexpressed in the cancerous tissue.

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Additionally, as Elledge et al teach an mRNA with the same nucleotide sequence as the instantly claimed nucleic acid sequence there is a reasonable expectation of success in detecting and comparing expression profiles of said polynucleotide by the methods of Carr and Von Knebel Doebertiz.

With regard to claims 5 and 6, it is noted that Von Knebel Doebertiz et al do not expressly teach that the normal tissue expression profile is an "average" expression profile of said nucleic acid from cancer-free subjects. Nevertheless, it would have been prima facie obvious to one ordinarily skilled in the art at the time the invention was made to measure the expression profile of said at least one nucleic acid in more than one reference biological sample, and then determine the average value of the expression profiles of that nucleic acid in the samples, so as to compare the expression profile of the nucleic acid in the colon cancer tissue and the average value in cancer-free colon tissue or to compare the expression profile of the nucleic acid in the lung cancer tissue and the average value in cancer-free lung tissue, because it would be recognized that the average value better reflects the standard level of expression in normal, non-cancerous colon or lung tissues. This is because it would be expected that the normal level of expression of any nucleic acid will vary in normal subjects, at least to some extent, such that the difference in the levels of expression in the colon or lung cancer tissue and any one specimen of the corresponding normal tissue might be more or less

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significant, which could lead the practitioner of the process to falsely conclude that the nucleic acid is or is not overexpressed in the cancerous tissue. Therefore, one ordinarily skilled in the art at the time the invention was made to would have been motivated to do so in order to more accurately determine whether or not the nucleic acid is overexpressed in the colon or lung cancer tissue, relative to the standard level of expression that occurs in the corresponding normal tissues.

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Because Carr teaches the expression profiles are determined using RT-PCR or nucleic acid array, it would have been *prima facie* obvious to determine the average value of the expression profiles of that nucleic acid in the samples using such methodology. One ordinarily skilled in the art would have been motivated to do so because such methodology was both routine and conventional at the time the invention was made, and was recognized to be very sensitive.

Thus, there would be an advantage and a reasonable expectation of success in detecting an expression profile of a nucleic acid comprising SEQ ID NO:1 in a colon cancer tissue from a human subject and comparing said expression profile to an average expression profile of a nucleic acid comprising SEQ ID NO:1 from colon tissue obtained from cancer-free subjects or in detecting an expression profile of a nucleic acid comprising SEQ ID NO:1 in a lung cancer tissue from a human subject and comparing said expression profile to an average expression profile of a nucleic acid comprising SEQ ID NO:1 from lung tissue obtained from cancer-free subjects using RT-PCR or nucleic acid array, to determine whether said nucleic acid is overexpressed in the cancer tissue, respectively, in view of US Patent and US Patent 6,632,936, US Patent 7,101,985 and US Patent 6,709,832.

19. Claims 1, 5-7, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 7,081,340 (Baker et al, published 2006), in view of US Patent 6,709,832 (Von Knebel Doebertiz et al, published 2004).

The claims are herein drawn to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:12 in a colon cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:12 from normal colon tissue to determine whether said nucleic acid is overexpressed in the cancer tissue or to methods comprising detecting an expression profile of a nucleic acid comprising SEQ ID NO:12 in a lung cancer tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:12 from normal lung tissue to determine whether said nucleic acid is overexpressed in the cancer tissue. Claims 5 and 6 are further drawn to the method of claim 1, wherein the normal tissue reference profile is an average expression profile of said at least one nucleic acid in a plurality of reference biological samples of cancer-free subjects and wherein said expression profiles are determined using RT-PCR or nucleic acid arrays.

Baker et al teach methods of detecting an expression profile of an mRNA comprising SEQ ID NO:295 in colon cancer tissue that is 100% identical<sup>5</sup> to the instantly claimed SEQ ID NO:12 and comparing said expression profile to the expression profile of an mRNA comprising SEQ ID NO:295 from a cancer tissue reference expression profile set. Baker et al also teach methods of detecting an expression profile of an mRNA comprising SEQ ID NO:295 in lung cancer tissue that is 100% identical to the instantly claimed SEQ ID NO:12 and comparing said expression profile to the expression profile of an mRNA comprising SEQ ID NO:295 from a cancer tissue reference expression profile set; see entire document (e.g., column 2, lines 34-44, column 5, lines, 43-63) Baker et al also teach said expression profiles being determined using RT-PCR (see e.g., column 4, lines 43-60).

Baker et al do not expressly teach comparing the lung or colon cancer tissue expression profile to a corresponding normal tissue reference profile.

This deficiency is made up for in the teachings of Von Knebel Doebertiz et al.

Von Knebel Doebertiz et al teach that it is an obvious thing to compare an mRNA

<sup>&</sup>lt;sup>5</sup> See the alignment of these sequences attached here as Exhibit D.

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expression profile from a cancerous body sample with a corresponding mRNA expression profile from a body sample which originates from a healthy person) (see entire document, e.g., column 2 lines 45-48 and 59-60).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to compare the expression profile of an mRNA comprising SEQ ID NO:12 in lung cancer tissues to the expression profile of an mRNA comprising SEQ ID NO:12 in corresponding normal lung tissue from subjects without cancer or to compare the expression profile of an mRNA comprising SEQ ID NO:12 in colon cancer tissues to the expression profile of an mRNA comprising SEQ ID NO:12 in corresponding normal colon tissue from subjects without cancer, in order to compare the expression profiles to determine whether said mRNA is overexpressed in the cancer tissue.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to detect an expression profile of a nucleic acid comprising SEQ ID NO:12 in a colon or lung cacner tissue from a human subject and comparing said expression profile to the expression profile of a nucleic acid comprising SEQ ID NO:12 from normal colon or lung tissue, respectively to determine whether said nucleic acid is overexpressed in the cancer tissue because Baker et al teach methods of detecting an mRNA that is 100% identical to SEQ ID NO:12 in colon and lung cancer tissue and Von Knebel Doebertiz et al teach that it is obvious to compare a tissue suspected of being cancerous with a corresponding normal tissue, in order to detect cancer markers overexpressed in the cancerous tissue.

With regard to claims 5 and 6, it is noted that Von Knebel Doebertiz et al do not expressly teach that the normal tissue expression profile is an "average" expression profile of said nucleic acid from cancer-free subjects. Nevertheless, it would have been prima facie obvious to one ordinarily skilled in the art at the time the invention was made to measure the expression profile of said at least one nucleic acid in more than one reference biological sample, and then determine the average value of the expression profiles of that nucleic acid in the samples, so as to compare the expression profile of

the nucleic acid in the colon cancer tissue and the average value in cancer-free colon tissue or to compare the expression profile of the nucleic acid in the lung cancer tissue and the average value in cancer-free lung tissue, because it would be recognized that the average value better reflects the standard level of expression in normal, non-cancerous colon or lung tissues. This is because it would be expected that the normal level of expression of any nucleic acid will vary in normal subjects, at least to some extent, such that the difference in the levels of expression in the colon or lung cancer tissue and any one specimen of the corresponding normal tissue might be more or less significant, which could lead the practitioner of the process to falsely conclude that the nucleic acid is or is not overexpressed in the cancerous tissue. Therefore, one ordinarily skilled in the art at the time the invention was made to would have been motivated to do so in order to more accurately determine whether or not the nucleic acid is overexpressed in the colon or lung cancer tissue, relative to the standard level of expression that occurs in the corresponding normal tissues.

Because Baker et al teach the expression profiles are determined using RT-PCR, it would have been *prima facie* obvious to determine the average value of the expression profiles of that nucleic acid in the samples using such methodology. One ordinarily skilled in the art would have been motivated to do so because such methodology was both routine and conventional at the time the invention was made, and was recognized to be very sensitive. Additionally, it is noted that Baker et al do not expressly teach using nucleic assay arrays to determine said expression profiles. Nevertheless, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to measure the expression profiles by nucleic assay array or by RT-PCR as both technologies were recognized to be used in methods to provide mRNA expression profiles. One ordinarily skilled in the art would have been motivated to do so because both methodologies were routine and conventional at the time the invention was made, and were recognized to be used in methods to determine mRNA expression profiles.

Thus, there would be an advantage and a reasonable expectation of success in detecting an expression profile of a nucleic acid comprising SEQ ID NO:12 in a colon

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cancer tissue from a human subject and comparing said expression profile to an average expression profile of a nucleic acid comprising SEQ ID NO:12 from colon tissue obtained from cancer-free subjects or in detecting an expression profile of a nucleic acid comprising SEQ ID NO:12 in a lung cancer tissue from a human subject and comparing said expression profile to an average expression profile of a nucleic acid comprising SEQ ID NO:12 from lung tissue obtained from cancer-free subjects using RT-PCR or nucleic acid array, to determine whether said nucleic acid is overexpressed in the cancer tissue, respectively, in view of US Patent 7,081,340 and US Patent 6,709,832.

#### Conclusion

- 20. No claim is allowed.
- 21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM

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with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <a href="http://pair-direct.uspto.gov">http://pair-direct.uspto.gov</a>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully, Brad Duffy 571-272-9935 /Stephen L. Rawlings/ Stephen L. Rawlings, Ph.D. Primary Examiner, Art Unit 1643

bd August 17, 2007

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Exhib+ A
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    markers for diagnosing e.g. cancer, ischemia or heart diseases, or as
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    therapeutic targets for screening drugs for treating these diseases.
XX
PS
    Claim 8; Page 641; 767pp; English.
XX
    The present invention describes an isolated nucleic acid molecule, which
CC
CC
    comprises the sequence of any of the genes that are up-regulated or down-
    regulated in specific cancers (e.g. about 1031 genes up-regulated in
CC
CC
    acute lymphocytic leukemia). ACC72641 to ACC72860 represent cancer
    related gene nucleotide sequences which encode the proteins given in
    ABR58521 to ABR58709. Also described: (1) determining the presence or
CC
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    absence of a pathological cell in a patient; (2) an expression vector
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    comprising a nucleic acid molecule described above; (3) a host cell
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    comprising the vector; (4) an isolated polypeptide, which is encoded by
CC
    the nucleic acid; (5) an antibody that specifically binds the polypeptide
    of (4); (6) specifically targeting a compound to a pathological cell in a
CC
CC
    patient by administering to the patient the antibody above; and (7) a
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    drug screening assay. The nucleic acid is useful as diagnostic markers or
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CC
   diagnosing a pathology, e.g. cancer (e.g. cancer of the bone marrow,
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    pancreas, prostate, skin and uterus), wounds, ischaemia, heart diseases,
CC
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    atherosclerosis and endometriosis. The nucleic acid is also useful in
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    drug screening, particularly for identifying agents for treating these
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  CURRENT FILING DATE: 1999-05-11
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Db	126	51	CCCACTTTATGCAGCTTTGAAAATGGAAAGTATGGAAATCATTGAGGAGATTCAATGCCA	1320
Qλ	134	7	AACTCAACAGGAAAACCTCAGCAGTAATAGTGATGGAATATCACCCAAAAGGCGTCGTCT	1406
Dk	132	21	AACTCAACAGGAAAACCTCAGCAGTAATAGTGATGGAATATCACCCAAAAAGGCGTCGTCT	1380
Qy	140	7	CAGCTCGTCTCTAAACCCTTCTAAAAGAGCACCAAAACAGACTGAGGAAATTAAACATGT	1466
Dk	138	31	CAGCTCGTCTCTAAAACCCTTCTAAAAGAGCACCAAAACAGACTGAGGAAATTAAACATGT	1440
Q۷	146	57	GGACATGAACCAAAAGAGCATATTATGGAGTGCACTGAAACAGAAAGCTGAATCCCTTCA	1526
Dk	144	1	GGACATGAACCAAAAGAGCATATTATGGAGTGCACTGAAACAGAAAGCTGAATCCCTTCA	1500
QΣ	152	27	GATTTCCCTTGAATACAGTGGCCTAAAGAATCCTGTTATTGAGATGTTAGAAGGAATTGC	1586
Dk	150	1	GATTTCCCTTGAATACAGTGGCCTAAAGAATCCTGTTATTGAGATGTTAGAAGGAATTGC	1560
QΣ	158	37	TGTTGTCTTACAACTGACTGCTCTGTGTACTGTTCATTGTTCTCAAAACATGAACTG	1646
Dk	156	51	TGTTGTCTTACAACTGACTGCTCTGTGTACTGTTCATTGTTCTCATCAAAACATGAACTG	1620
Q١	164	7	CCGTACTTCAAGGACTGTCAACATAAATCCAAGAAGAAACCTTCTGTAGTGATAACTTG	1706
Dk	162	21	CCGTACTTTCAAGGACTGTCAACATAAATCCAAGAAGAAACCTTCTGTAGTGATAACTTG	1680
δ7	170	7	GATGTCATTGGATTTTTACACAAAAGTGCTTAAGAGCTGTAGAAGTTTGTTAGAATCTGT	1766
DŁ	168	31		1740
Qλ	176	57	TCAGAAACTGGACCTGGAGGCAACCATTGATAAGGTGGTGAAAATTTATGATGCTTTGAT	1826
Db	174	1	TCAGAAACTGGACCTGGAGGCAACCATTGATAAGGTGGTGAAAATTTATGATGCTTTGAT	1800
Qλ	182	27	TTATATGCAAGTAAACAGTTCATTTGAAGATCATATCCTGGAAGATTTATGTGGTATGCT	1886
Db	180	1	${\tt TTATATGCAAGTAAACAGTTCATTTGAAGATCATATCCTGGAAGATTTATGTGGTATGCT}$	1860

Qу	1887	CTCACTTCCATGGATTTATTCCCATTCTGATGATGGCTGTTTAAAGTTGACCACATTTGC	1946
Db	1861	CTCACTTCCATGGATTTATTCCCATTCTGATGATGGCTGTTTAAAGTTGACCACATTTGC	1920
Qу	1947	CGCTAATCTTCTAACATTAAGCTGTAGGATTTCAGATAGCTATTCACCACAGGCACAATC	2006
Db	1921	CGCTAATCTTCTAACATTAAGCTGTAGGATTTCAGATAGCTATTCACCACAGGCACAATC	1980
Qу	2007	ACGATGTGTGTTTCTGACTCTGTTTCCAAGAAGAATATTCCTTGAGTGGAGAACAGC	2066
Db	1981	ACGATGTGTGTTTCTTGACTCTGTTTCCAAGAAGAATATTCCTTGAGTGGAGAACAGC	2040
Qу		AGTTTACAACTGGGCCCTGCAGAGCTCCCATGAAGTAATCCGGGCTAGTTGTGTTAGTGG	
Db		AGTTTACAACTGGGCCCTGCAGAGCTCCCATGAAGTAATCCGGGCTAGTTGTGTTAGTGG .	
Qу		ATTTTTTATCTTATTGCAGCAGCAGAATTCTTGTAACAGAGTTCCCAAGATTCTTATAGA	
Db		ATTTTTTATCTTATTGCAGCAGCAGAATTCTTGTAACAGAGTTCCCAAGATTCTTATAGA	
Qу		TAAAGTCAAAGATGATTCTGACATTGTCAAGAAAGAATTTGCTTCTATACTTGGTCAACT	
Db		TAAAGTCAAAGATGATTCTGACATTGTCAAGAAAGAATTTGCTTCTATACTTGGTCAACT	2220
Qу		TGTCTGTACTCTTCACGGCATGTTTTATCTGACAAGTTCTTTAACAGAACCTTTCTCTGA	
Db		TGTCTGTACTCTTCACGGCATGTTTTATCTGACAAGTTCTTTAACAGAACCTTTCTCTGA	
Qy Db		ACACGGACATGTGGACCTCTTCTGTAGGAACTTGAAAGCCACTTCTCAACATGAATGTTC	
Qy		ATCTTCTCAACTAAAAGCTTCTGTCTGCAAGCCATTCCTTTTCCTACTGAAAAAAAA	
Db		ATCTTCTCAACTAAAAGCTTCTGTCTGCAAGCCATTCCTTTTCCTACTGAAAAAAAA	
Qy		ACCTAGTCCAGTAAAACTTGCTTTCATAGATAATCTACATCATCTTTGTAAGCATCTTGA	
Db		ACCTAGTCCAGTAAAACTTGCTTTCATAGATAATCTACATCATCTTTGTAAGCATCTTGA	
Qy	2487	TTTTAGAGAAGATGAAACAGATGTAAAAGCAGTTCTTGGAACTTTATTAAATTTAATGGA	2546
Db	2461		2520
Qу	2547	AGATCCAGACAAAGATGTTAGAGTGGCTTTTAGTGGAAATATCAAGCACATATTGGAATC	2606
Db	2521		2580
Qу		CTTGGACTCTGAAGATGGATTTATAAAGGAGCTTTTTGTCTTAAGAATGAAGGAAG	2666
Db			2640
Qy	. 2667	TACACATGCCCAAATATCAAGAAATAATGAGCTGAAGGATACCTTGATTCTTACAACAGG	2726
Db	2641	TACACATGCCCAAATATCAAGAAATAATGAGCTGAAGGATACCTTGATTCTTACAACAGG	2700
Qу	2727	GGATATTGGAAGGGCCGCAAAAGGAGATTTGGTACCATTTGCACTCTTACACTTATTGCA	2786
Db	2701	GGATATTGGAAGGGCCGCAAAAGGAGATTTGGTACCATTTGCACTCTTACACTTATTGCA	2760
Qy	2787	TTGTTTGTTATCCAAGTCAGCATCTGTCTCTGGAGCAGCATACACAGAAATTAGAGCTCT	2846
Db	2761	TTGTTTGTTATCCAAGTCAGCATCTGTCTCTGGAGCAGCATACACAGAAATTAGAGCTCT	2820
Qу	2847	GGTTGCAGCTAAAAGTGTTAAACTGCAAAGTTTTTTCAGCCAGTATAAGAAACCCATCTG	2906
Db	2821	GGTTGCAGCTAAAAGTGTTAAACTGCAAAGTTTTTTCAGCCAGTATAAGAAACCCATCTG	2880
Qу		TCAGTTTTTGGTAGAATCCCTTCACTCTAGTCAGATGACAGCACTTCCGAATACTCCATG	
Db		TCAGTTTTTGGTAGAATCCCTTCACTCTAGTCAGATGACAGCACTTCCGAATACTCCATG	
Qγ		CCAGAATGCTGACGTGCGAAAACAAGATGTGGCTCACCAGAGAGAAATGGCTTTAAATAC	
Db	2941	CCAGAATGCTGACGTGCGAAAACAAGATGTGGCTCACCAGAGAGAAATGGCTTTAAATAC	3000

		•	
Qy Db		GTTGTCTGAAATTGCCAACGTTTTCGACTTTCCTGATCTTAATCGTTTTCTTACTAGGAC	
			3146
Dp .		ATTACAAGTTCTACTACTGATCTTGCTGCCAAAGCAAGCCCTGCAGCTTCTGCTCTCAT ATTACAAGTTCTACTACCTGATCTTGCTGCCAAAGCAAGC	
Qy	3147	TCGAACTTTAGGAAAACAATTAAATGTCAATCGTAGAGAGATTTTAATAAACAACTTCAA	3206
Db	3121		3180
Qy .	3207	ATATATTTTTCTCATTTGGTCTGTTCTTGTTCCAAAGATGAATTAGAACGTGCCCTTCA	3266
Db	3181	ATATATTTTŢCTCATTTGGTCTGTTCTTGTTCCAAAGATGAATTAGAACGTGCCCTTCA	3240
QУ	3267	TTATCTGAAGAATGAAACAGAAATTGAACTGGGGAGCCTGTTGAGACAAGATTTCCAAGG	3326
Db	3241		3300
QУ	3327	ATTGCATAATGAATTATTGCTGCGTATTGGAGAACACTATCAACAGGTTTTTAATGGTTT	3386
Db	3301	ATTGCATAATGAATTATTGCTGCGTATTGGAGAACACTATCAACAGGTTTTTAATGGTTT	3360
Qу	3387	GTCAATACTTGCCTCATTTGCATCCAGTGATGATCCATATCAGGGCCCGAGAGATATCAT	3446
Db	3361	GTCAATACTTGCCTCATTTGCATCCAGTGATGATCCATATCAGGGCCCGAGAGATATCAT	3420
QУ	3447	ATCACCTGAACTGATGGCTGATTATTTACAACCCAAATTGTTGGGCATTTTTGGCTTTTTT	3506
Db .	3421	ATCACCTGAACTGATGGCTGATTATTTACAACCCAAATTGTTGGGCATTTTGGCTTTTTTT	3480
Qу	3507	TAACATGCAGTTACTGAGCTCTAGTGTTGGCATTGAAGATAAGAAAATGGCCTTGAACAG	3566
Db	3481	TAACATGCAGTTACTGAGCTCTAGTGTTGGCATTGAAGATAAGAAAATGGCCTTGAACAG	3540
Qу	3567	TTTGATGTCTTTGATGAAGTTAATGGGACCCAAACATGTCAGTTCTGTGAGGGTGAAGAT	3626
Db	3541	TTTGATGTCTTTGATGAAGTTAATGGGACCCAAACATGTCAGTTCTGTGAGGGTGAAGAT	3600
Qγ	3627	GATGACCACACTGAGAACTGGCCTTCGATTCAAGGATGATTTTCCTGAATTGTGTTGCAG	3686
Db	3601	GATGACCACACTGAGAACTGGCCTTCGATTCAAGGATGATTTTCCTGAATTGTGTTGCAG	3660
. ŌÀ	3687	AGCTTGGGACTGCTTTGTTCGCTGCCTGGATCATGCTTGTCTGGGCTCCCTTCTCAGTCA	3746
Db	3661	AGCTTGGGACTGCTTTGTTCGCTGCCTGGATCATGCTTGTCTGGGCTCCCTTCTCAGTCA	3720
Qy	3747	TGTAATAGTAGCTTTGTTACCTCTTATACACATCCAGCCTAAAGAAACTGCAGCTATCTT	3806
Db	3721	TGTAATAGTAGCTTTGTTACCTCTTATACACATCCAGCCTAAAGAAACTGCAGCTATCTT	3780-
Qy	3807	${\tt CCACTACCTCATAATTGAAAACAGGGATGCTGTGCAAGATTTTCTTCATGAAATATATTT}$	3866
Db	3781	CCACTACCTCATAATTGAAAACAGGGATGCTGCAAGATTTTCTTCATGAAATATATTT	3840
Qy	3867	TTTACCTGATCATCCAGAATTAAAAAAGATAAAAGCCGTTCTCCAGGAATACAGAAAGGA	3926
Db	3841	TTTACCTGATCATCCAGAATTAAAAAAGATAAAAGCCGTTCTCCAGGAATACAGAAAGGA	3900
Qу	3927	GACCTCTGAGAGCACTGATCTTCAGACAACTCTTCAGCTCTCTATGAAGGCCATTCAACA	3986
Db	3901	GACCTCTGAGAGCACTGATCTTCAGACAACTCTTCAGCTCTCTATGAAGGCCATTCAACA	3960
QУ	3987	TGAAAATGTCGATGTTCGTATTCATGCTCTTACAAGCTTGAAGGAAACCTTGTATAAAAA	4046
Db	3961	TGAAAATGTCGATGTTCGTATTCATGCTCTTACAAGCTTGAAGGAAACCTTGTATAAAAA	4020
Qy	4047	TCAGGAAAAACTGATAAAGTATGCAACAGACAGTGAAACAGTAGAACCTATTATCTCACA	4106
Db	4021	TCAGGAAAACTGATAAAGTATGCAACAGACAGTGAAACAGTAGAACCTATTATCTCACA	4080
Qу	4107	GTTGGTGACAGTGCTTTTGAAAGGTTGCCAAGATGCAAACTCTCAAGCTCGGTTGCTCTG	4166
.Db	4081	GTTGGTGACAGTGCTTTTGAAAGGTTGCCAAGATGCAAACTCTCAAGCTCGGTTGCTCTG	4140

Qy Db		TGGGGAATGTTTAGGGGAATTGGGGGCGATAGATCCAGGTCGATTAGATTTCTCAACAAC	
		TGAAACTCAAGGAAAAGATTTTACATTTGTGACTGGAGTAGAAGATTCAAGCTTTGCCTA	
ДЪ			
Qy	4287	TGGATTATTGATGGAGCTAACAAGAGCTTACCTTGCGTATGCTGATAATAGCCGAGCTCA	4346
Db	4261	TGGATTATTGATGGAGCTAACAAGAGCTTACCTTGCGTATGCTGATAATAGCCGAGCTCA	4320
Qу	4347	${\tt AGATTCAGCTGCCTATGCCATTCAGGAGTTGCTTTCTATTTATGACTGTAGAGAGATGGA}$	4406
Db	4321	AGATTCAGCTGCCTATGCCATTCAGGAGTTGCTTTCTATTTATGACTGTAGAGAGATGGA	4380
Qy ·	4407	GACCAACGGCCCAGGTCACCAATTGTGGAGGAGATTTCCTGAGCATGTTCGGGAAATACT	4466
Db	4381	GACCAACGGCCCAGGTCACCAATTGTGGAGGAGATTTCCTGAGCATGTTCGGGAAATACT	4440
Qу	4467	AGAACCTCATCTAAATACCAGATACAAGAGTTCTCAGAAGTCAACCGATTGGTCTGGAGT	4526
Db	. 4441.	AGAACCTCATCTAAATACCAGATACAAGAGTTCTCAGAAGTCAACCGATTGGTCTGGAGT	4500
Qу	4527	AAAGAAGCCAATTTACTTAAGTAAATTGGGTAGTAACTTTGCAGAATGGTCAGCATCTTG	4586
Db	4501	AAAGAAGCCAATTTACTTAAGTAAATTGGGTAGTAACTTTGCAGAATGGTCAGCATCTTG	4560
Qy	4587	${\tt GGCAGGTTATCTTATTACAAAGGTTCGACATGATCTTGCCAGTAAAATTTTCACCTGCTG}$	4646
Db	4561		4620
.Qy	4647	TAGCATTATGATGAAGCATGATTTCAAAGTGACCATCTATCT	4706
Db	4621	TAGCATTATGATGAAGCATGATTTCAAAGTGACCATCTATCT	4680
Qy	4707	GTATGTCTTACTGGGTTGTAATCAAGAAGATCAGCAGGAGGTTTATGCAGAAATTATGGC	4766
Db	4681		4740
Qу	4767	AGTTCTAAAGCATGACGATCAGCATACCATAAATACCCAAGACATTGCATCTGATCTGTG	4826
Db	4741	AGTTCTAAAGCATGACGATCAGCATACCATAAATACCCAAGACATTGCATCTGTG	4800
Qу	4827	${\tt TCAACTCAGTACACAGACTGTGTTCTCCATGCTTGACCATCTCACACAGTGGGCAAGGCA}$	4886
Db	4801	TCAACTCAGTACACAGACTGTGTTCTCCATGCTTGACCATCTCACACAGTGGGCAAGGCA	4860
Qу	4887	CAAATTTCAGGCACTGAAAGCTGAGAAATGTCCACACAGCAAATCAAACAGAAATAAGGT	4946
Db	4861	CAAATTCAGGCACTGAAAGCTGAGAAATGTCCACACAGCAAATCAAACAGAAATAAGGT	4920
Qу	4947	${\tt AGACTCAATGGTATCTACTGTGGATTATGAAGACTATCAGAGTGTAACCCGTTTTCTAGA}$	5006
Db	4921	AGACTCAATGGTATCTACTGTGGATTATGAAGACTATCAGAGTGTAACCCGTTTTCTAGA	4980
Qу	5007	${\tt CCTCATACCCCAGGATACTCTGGCAGTAGCTTCCTTTCGCTCCAAAGCATACACCGAGC}$	5066
Db	4981		5040
Qy	5067	$\tt TGTAATGCACTTTGAATCATTTATTACAGAAAAGAAGCAAAATATTCAGGAACATCTTGG$	5126
Db	5041		5100
Qу	5127	ATTTTTACAGAAATTGTATGCTGCTATGCATGAACCTGATGGAGTGGCCGGAGTCAGTGC	5186
Db '	5101		5160
Qy	5187	AATTAGAAAGGCAGAACCATCTCTAAAAGAACAGATCCTTGAACATGAAAGCCTTGGCTT	5246
Db	5161	AATTAGAAAGGCAGAACCATCTCTAAAAGAACAGATCCTTGAACATGAAAGCCTTGGCTT	5220
Qy	5247		5306
Db	5221	GCTGAGGGATGCCACTGCTTATGACAGGGCTATTCAGCTAGAACCAGACCAGATCAT	5280

QУ		TCATTATCATGTGTAGTAAAGTCCATGTTAGGTCTTGGTCAGCTGTCTACTGTTATCAC	
Db		TCATTATCATGGTGTAGTAAAGTCCATGTTAGGTCTTGGTCAGCTGTCTACTGTTATCAC	
ДУ		TCAGGTGAATGGAGTGCATGCTAACAGGTCCGAGTGGACAGATTAAACACGTACAG	
Db		TCAGGTGAATGGAGTGCATGCTAACAGGTCCGAGTGGACAGATGAATTAAACACGTACAG	
QY		AGTGGAAGCAGCTTGGAAATTGTCACAGTGGGATTTGGTGGAAAACTATTTGGCAGCAGA	
Db		AGTGGAAGCATTGGAAATTGTCACAGTGGGATTTGGTGGAAAACTATTTGGCAGCAGA	
QУ		TGGAAAATCTACAACATGGAGTGTCAGACTGGGACAGCTATTATTATCAGCCAAAAAAG	
Db		TGGAAAATCTACAACATGGAGTGTCAGACTGGGACAGCTATTATTATCAGCCAAAAAAAG	
Qy			5606
Db .	5521	AGATATCACAGCTTTTTATGACTCACTGAAACTAGTGAGAGCAGAACAAATTGTACCTCT	5580
QУ	5607	TTCAGCTGCAAGCTTTGAAAGAGGCTCCTACCAACGAGGATATGAATATATTGTGAGATT	5666
Db	5581	TTCAGCTGCAAGCTTTGAAAGAGGCTCCTACCAACGAGGATATGAATATATTGTGAGATT	5640
QУ	5667	GCACATGTTATGTGAGTTGGAGCATAGCATCAAACCACTTTTCCAGCATTCTCCAGGTGA	5726
Db	5641	GCACATGTTATGTGAGTTGGAGCATAGCATCAAACCACTTTTCCAGCATTCTCCAGGTGA	5700
Qy	5727	CAGTTCTCAAGAAGATTCTCTAAACTGGGTAGCTCGACTAGAAATGACCCAGAATTCCTA	5786
Db	5701	CAGTTCTCAAGAAGATTCTCTAAACTGGGTAGCTCGACTAGAAATGACCCAGAATTCCTA	5760
Qy	5787	CAGAGCCAAGGAGCCTATCCTGGCTCTCCGGAGGGCTTTACTAAGCCTCAACAAAAGACC	5846
Db	5761	.CAGAGCCAAGGACCCTATCCTGGCTCTCCGGAGGGCTTTACTAAGCCTCAACAAAAGACC	5820
QУ	5,847	AGATTACAATGAAATGGTTGGAGAATGCTGĢCTGCAGAGTGCCAGGGTAGCTAGAAAGGC	5906
Db	5821	AGATTACAATGAAATGGTTGGAGAATGCTGGCTGCAGAGTGCCAGGGTAGCTAGAAAGGC	5880
δλ .	5907	TGGTCACCACAGACAGCCTACAATGCTCTCCTTAATGCAGGGGAATCACGACTCGCTGA	5966
Db	5881	TGGTCACCACCAGACAGCCTACAATGCTCTCCTTAATGCAGGGGAATCACGACTCGCTGA	5940
QУ	5967	ACTGTACGTGGAAAGGGCAAAGTGGCTCTGGTCCAAGGGTGATGTTCACCAGGCACTAAT	6026
Db ',	5941		6000
Qy .	6027	TGTTCTTCAAAAAGGTGTTGAATTATGTTTTCCTGAAAATGAAACCCCACCTGAGGGTAA	6086
Db	6001	TGTTCTTCAAAAAGGTGTTGAATTATGTTTTCCTGAAAATGAAACCCCACCTGAGGGTAA	6060
Qу	6087	GAACATGTTAATCCATGGTCGAGCTATGCTACTAGTGGGCCGATTTATGGAAGAACAGC	6146
Db	6061		6120
QУ	6147	TAACTTTGAAAGCAATGCAATTATGAAAAAATATAAGGATGTGACCGCGTGCCTGCC	6206
Db	6121	TAACTTTGAAAGCAATGCAATTATGAAAAAATATAAGGATGTGACCGCGTGCCTGCC	6180
Qy	6207	ATGGGAGGATGGCCATTTTTACCTTGCCAAGTACTATGACAAATTGATGCCCATGGTCAC	6266
Db .	6181	ATGGGAGGATGGCCATTTTTACCTTGCCAAGTACTATGACAAATTGATGCCCATGGTCAC	6240
Qу	6267	${\tt AGACAACAAAATGGAAAAGCAAGGTGATCTCATCCGGTATATAGTTCTTCATTTTGGCAG}$	6326
Db	6241	AGACAACAAAATGGAAAAGCAAGGTGATCTCATCCGGTATATAGTTCTTCATTTTGGCAG	6300
Qy	6327	ATCTCTACAATATGGAAATCAGTTCATATATCAGTCAATGCCACGAATGTTAACTCTATG	6386
Db	6301	ATCTCTACAATATGGAAATCAGTTCATATATCAGTCAATGCCACGAATGTTAACTCTATG	6360
Qу	6387	GCTTGATTATGGTACAAAGGCATATGAATGGGAAAAAGCTGGCCGCTCCGATCGTGTACA	6446
Db	6361	GCTTGATTATGGTACAAAGGCATATGAATGGGAAAAAGCTGGCCGCTCCGATCGTGTACA	6420

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Qу	6447	AATGAGGAATGATTTGGGTAAAATAAACAAGGTTATCACAGAGCATACAAACTATTTAGC	6506
Db	6421	AATGAGGAATGATTTGGGTAAAATAAACAAGGTTATCACAGAGCATACAAACTATTTAGC	6480
Qу		TCCATATCAATTTTTGACTGCTTTTTCACAATTGATCTCTCGAATTTGTCATTCTCACGA	
Db		TCCATATCAATTTTTGACTGCTTTTTCACAATTGATCTCTCGAATTTGTCATTCTCACGA	
Qу		TGAAGTTTTTGTTGTCTTGATGGAAATAATAGCCAAAGTATTTCTAGCCTATCCTCAACA	
Db		TGAAGTTTTTGTTGTTGATGGAAATAATAGCCAAAGTATTTCTAGCCTATCCTCAACA	
Qу		AGCAATGTGGATGATGACAGCTGTGTCAAAGTCATCTTATCCCATGCGTGTGAACAGATG	
Db		AGCAATGTGGATGATGACAGCTGTGTCAAAGTCATCTTATCCCATGCGTGTGAACAGATG	
Qу		CAAGGAAATCCTCAATAAAGCTATTCATATGAAAAAATCCTTAGAGAAGTTTGTTGGAGA	
Db		CAAGGAAATCCTCAATAAAGCTATTCATATGAAAAAATCCTTAGAGAAGTTTGTTGGAGA	
Qу		TGCAACTCGCCTAACAGATAAGCTTCTAGAATTGTGCAATAAACCGGTTGATGGAAGTAG	
Db		TGCAACTCGCCTAACAGATAAGCTTCTAGAATTGTGCAATAAACCGGTTGATGGAAGTAG	
Qу		TTCCACATTAAGCATGAGCACTCATTTTAAAATGCTTAAAAAGCTGGTAGAAGAAGCAAC	
Db		TTCCACATTAAGCATGAGCACTCATTTTAAAATGCTTAAAAAGCTGGTAGAAGAAGCAAC  ATTTAGTGAAATCCTCATTCCTCTACAATCAGTCATGATACCTACACTTCCATCAATTCT	
Qy Db		ATTTAGTGAAATCCTCATTCCTCTACAATCAGTCATGATACCTACACTTCCATCAATTCT	
		GGGTACCCATGCTAACCATGCTAGCCATGAACCATTCCTGGACATTGGGCCTATATTGC	
Qy Db		GGGTACCCATGCTAACCATGCTAGCCATGAACCATTTCCTGGACATTGGGCCTATATTGC	
Qу		AGGGTTTGATGATATGGTGGAAATTCTTTGCTTCTCTTCAGAAACCAAAGAAGATTTCTTT	
Db		AGGGTTTGATGATATGGTGGAAATTCTTGCTTCTCTTCAGAAACCAAAGAAGATTTCTTT	
Qу	7047	AAAAGGCTCAGATGGAAAGTTCTACATCATGATGTGTAAGCCAAAAGATGACCTGAGAAA	7106
Db	7021		7080
Qу	7107	GGATTGTAGACTAATGGAATTCAATTCCTTGATTAATAAGTGCTTAAGAAAAGATGCAGA	7166
Db	7081		7140
Qу	7167	GTCTCGTAGAAGAACTTCATATTCGAACATATGCAGTTATTCCACTAAATGATGAATG	7226
Db	7141		7200
Qу	`7227	${\tt TGGGATTATTGAATGGGTGAACAACACTGCTGGTTTGAGACCTATTCTGACCAAACTATA}$	7286
Db	. 7201	TGGGATTATTGAATGGGTGAACAACACTGCTGGTTTGAGACCTATTCTGACCAAACTATA	7260
Qy	7287	TAAAGAAAAGGGAGTGTATATGACAGGAAAAGAACTTCGCCAGTGTATGCTACCAAAGTC	7346
Db	7261	TAAAGAAAAGGGAGTGTATATGACAGGAAAAGAACTTCGCCAGTGTATGCTACCAAAGTC	7320
QУ	7347	AGCAGCTTTATCTGAAAAACTCAAAGTATTCCGAGAATTTCTCCTGCCCAGGCATCCTCC	7406
Db	7,321	AGCAGCTTTATCTGAAAAACTCAAAGTATTCCGAGAATTTCTCCTGCCCAGGCATCCTCC	7380
Дλ	7407	TATTTTCATGAGTGGTTTCTGAGAACATTCCCTGATCCTACATCATGGTACAGTAG	7466
Db	7381	TATTTTCATGAGTGGTTTCTGAGAACATTCCCTGATCCTACATCATGGTACAGTAGTAG	7440
Qу	A •	ATCAGCTTACTGCCGTTCCACTGCAGTAATGTCAATGGTTGGT	
Db		ATCAGCTTACTGCCGTTCCACTGCAGTAATGTCAATGGTTGGT	
Qу		AGACCGTCATGGTGAAAATATTCTCTTTGATTCTTTGACTGGTGAATGCGTACATGTAGA	
Db	7501	AGACCGTCATGGTGAAAATATTCTCTTTGATTCTTTGACTGGTGAATGCGTACATGTAGA	7560

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Qу	7587	TTTCAATTGTCTTTTCAATAAGGGAGAAACCTTTGAAGTTCCAGAAATTGTGCCATTTCG 7646
Db	7561	TTTCAATTGTCTTTTCAATAAGGGAGAAACCTTTGAAGTTCCAGAAATTGTGCCATTTCG 7620
Qу	7647	CCTGACTCATAATATGGTTAATGGAATGGGTCCTATGGGAACAGAGGGTCTTTTTCGAAG 7706
Db	7621	CCTGACTCATAATATGGTTAATGGAATGGGTCCTATGGGAACAGAGGGTCTTTTTCGAAG 7680
QΥ.	7707	AGCATGTGAAGTTACAATGAGGCTGATGCGTGATCAGCGAGAGCCTTTAATGAGTGTCTT 7766
Db	7681	
Qу	7767	AAAGACTTTTCTACATGATCCTCTTGTGGAATGGAGTAAACCAGTGAAAGGGCATTCCAA 7826
Db	7741	AAAGACTTTCTACATGATCCTCTTGTGGAATGGAGTAAACCAGTGAAAGGGCATTCCAA 7800
Qy	7827	AGCGCCACTGAATGAAACTGGAGAAGTTGTCAATGAAAAGGCCAAGACCCATGTTCTTGA 7886
Db	7801	AGCGCCACTGAATGAAACTGGAGAAGTTGTCAATGAAAAGGCCAAGACCCATGTTCTTGA 7860
Qу	7887	CATTGAGCAGCGACTACAAGGTGTAATCAAGACTCGAAATAGAGTGACAGGACTGCCGTT 7946
Db	7861	
Qy	7947	ATCTATTGAAGGACATGTGCATTACCTTATACAAGAAGCTACTGATGAAAACTTACTATG 8006
Db	7921	
Ωу	8007	CCAGATGTATCTTGGTTGGACTCCATATATGTGAAATGAAATTATGTAAAAGAATATGTT 8066
Db	7981	
Qy .	8067	AATAATCTAAAAGTAATGCATTTGGTATGAATCTGTGGTTGTATCTGTTCAATTCTAAAG 8126
Db	8041	AATAATCTAAAAGTAATGCATTTGGTATGAATCTGTGGTTGTATCTGTTCAATTCTAAAG 8100
Qу	8127	TACAACATAAATTTACGTTCTCAGCAACTGTTATTTCTCTCTGATCATTAATTA
Db	8101	TACAACATAAATTTACGTTCTCAGCAACTGTTATTTCTCTCTGATCATTAATTA
Ωу	8187	AAATAATATACATTCAGTTATTAAGAAATAAACTGCTTTCTTAATAAAAAAAA
Db	8161	
Qy	8247	АААААААААААААААА 8265
Db	8221	
EndF</td <td></td> <td></td>		

## Exhibit C

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<!--StartFragment-->RESULT 01
US-10-300-453B-38
; Sequence 38, Application US/10300453B
 Patent No. 7101985
 GENERAL INFORMATION:
  APPLICANT: ELLEDGE, STEPHEN J.
  APPLICANT: CORTEZ, DAVID K.
           ZOU. LEE
  APPLICANT:
  TITLE OF INVENTION: METHODS AND COMPOSITIONS IN CHECKPOINT SIGNALING
  FILE REFERENCE: P02339US1
  CURRENT APPLICATION NUMBER: US/10/300,453B
  CURRENT FILING DATE:
                   2002-11-20
  PRIOR APPLICATION NUMBER: 60/331,821
  PRIOR FILING DATE: 2001-11-20
  NUMBER OF SEQ ID NOS: 50
  SOFTWARE: PatentIn Ver. 2.1
 SEQ ID NO 38
   LENGTH: 8265
   TYPE: DNA
   ORGANISM: Homo sapiens
US-10-300-453B-38
 Query Match
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 Best Local Similarity
                   100.0%; Pred. No. 0;
 Matches 8265; Conservative
                         0; Mismatches
                                          Indels
                                                     Gaps
                                                           0;
         1 GCCTCCACACGGCTCCGTCGGGCGCCGCTCTTCCGGCAGCGGTACGTTTGGAGACGCC 60
Qу
           1 GCCTCCACACGGCTCCGTCGGCCGCCTCTTCCGGCAGCGGTACGTTTGGAGACGCC 60
Db
Qy
        61 GGGAACCCGCGTTGGCGTGGTTGACTAGTGCCTCGCAGCCTCAGCATGGGGGAACATGGC 120
           Db
        61 GGGAACCCGCGTTGGCGTGGTTGACTAGTGCCTCGCAGCCTCAGCATGGGGGAACATGGC 120
       121 CTGGAGCTGGCTTCCATGATCCCCGCCCTGCGGGAGCTGGGCAGTGCCACACCAGAGGAA 180
Qу
           121 CTGGAGCTGGCTTCCATGATCCCCGCCCTGCGGGAGCTGGGCAGTGCCACACCAGAGGAA 180
Db
       181 TATAATACAGTTGTACAGAAGCCAAGACAAATTCTGTGTCAATTCATTGACCGGATACTT 240
Qν
           TATAATACAGTTGTACAGAAGCCAAGACAAATTCTGTGTCAATTCATTGACCGGATACTT 240
Db
       241 ACAGATGTAAATGTTGTTGCTGTAGAACTTGTAAAGAAAACTGACTCTCAGCCAACCTCC 300
Qу
           Db
       241 ACAGATGTAAATGTTGTTGCTGTAGAACTTGTAAAGAAAACTGACTCTCAGCCAACCTCC 300
       301 GTGATGTTGCTTGATTTCATCCAGCATATCATGAAATCCTCCCCACTTATGTTTGTAAAT 360
Qγ
           Db
       301 GTGATGTTGCTTGATTTCATCCAGCATATCATGAAATCCTCCCCACTTATGTTTGTAAAT 360
       361 GTGAGTGGAAGCCATGAGCGCAAAGGCAGTTGTATTGAATTCAGTAATTGGATCATAACG 420
Qу
           361 GTGAGTGGAAGCCATGAGCGCAAAGGCAGTTGTATTGAATTCAGTAATTGGATCATAACG 420
Db
       421 AGACTTCTGCGGATTGCAGCAACTCCCTCCTGTCATTTGTTACACAAGAAATCTGTGAA 480
Qy
           Db
          AGACTTCTGCGGATTGCAGCAACTCCCTCCTGTCATTTGTTACACAAGAAAATCTGTGAA 480
       481 GTCATCTGTTCATTATTATTTCTTTTAAAAGCAAGAGTCCTGCTATTTTTTGGGGTACTC 540
Qy
           481 GTCATCTGTTCATTATTATTTTCTTTTTAAAAGCAAGAGTCCTGCTATTTTTGGGGTACTC 540
Db
       541 ACAAAAGAATTATTACAACTTTTTGAAGACTTGGTTTACCTCCATAGAAGAAATGTGATG 600
Qу
           Db
          ACAAAAGAATTATTACAACTTTTTGAAGACTTGGTTTACCTCCATAGAAGAAATGTGATG 600
       601 GGTCATGCTGTGGAATGGCCAGTGGTCATGAGCCGATTTTTAAGTCAATTAGATGAACAC 660
Qγ
           601 GGTCATGCTGTGGAATGGCCAGTGGTCATGAGCCGATTTTTAAGTCAATTAGATGAACAC 660
       661 ATGGGATATTTACAATCAGCTCCTTTGCAGTTGATGAGTATGCAAAATTTAGAATTTATT 720
Qу
           661 ATGGGATATTTACAATCAGCTCCTTTGCAGTTGATGAGTATGCAAAATTTAGAATTTATT 720
Db
       721 GAAGTCACTTTATTAATGGTTCTTACTCGTATTATTGCAATTGTGTTTTTTAGAAGGCAA 780
Qу
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Db	721	GAAGTCACTTTATTAATGGTTCTTACTCGTATTATTGCAATTGTGTTTTTTAGAAGGCAA	780
Qу	. 781	GAACTCTTACTTTGGCAGATAGGTTGTTCTGCTAGAGTATGGTAGTCCAAAAATTAAA	840
Db	781	GAACTCTTACTTTGGCAGATAGGTTGTGTTCTGCTAGAGTATGGTAGTCCAAAAATTAAA	840
Qу	841	TCCCTAGCAATTAGCTTTTTAACAGAACTTTTTCAGCTTGGAGGACTACCAGCACCA	900
Db	841	TCCCTAGCAATTAGCTTTTTAACAGAACTTTTTCAGCTTGGAGGACTACCAGCACAACCA	900
Qу	901	GCTAGCACTTTTTCAGCTCATTTTTGGAATTATTAAAACACCTTGTAGAAATGGATACT	960
Db	901	GCTAGCACTTTTTCAGCTCATTTTTGGAATTATTAAAACACCTTGTAGAAATGGATACT	960
Qу	961	GACCAATTGAAACTCTATGAAGAGCCATTATCAAAGCTGATAAAGACACTATTTCCCTTT	1020
Db	, 961	GACCAATTGAAACTCTATGAAGAGCCATTATCAAAGCTGATAAAGACACTATTTCCCTTT	1020
Qу	1021	GAAGCAGAAGCTTATAGAAATATTGAACCTGTCTATTTAAATATGCTGCTGGAAAAACTC	1080
Db	. 1021	GAAGCAGAAGCTTATAGAAATATTGAACCTGTCTATTTAAATATGCTGCTGGAAAAACTC	1080
Qу	1081	TGTGTCATGTTTGAAGACGGTGTGCTCATGCGGCTTAAGTCTGATTTGCTAAAAGCAGCT	1140
Db	1081	TGTGTCATGTTTGAAGACGGTGTGCTCATGCGGCTTAAGTCTGATTTGCTAAAAGCAGCT	1140
Qу	1141	TTGTGCCATTTACTGCAGTATTTCCTTAAATTTGTGCCAGCTGGGTATGAATCTGCTTTA	1200
Db	1141	TTGTGCCATTTACTGCAGTATTTCCTTAAATTTGTGCCAGCTGGGTATGAATCTGCTTTA	1200
Qy		CAAGTCAGGAAGGTCTATGTGAGAAATATTTGTAAAGCTCTTTTGGATGTGCTTGGAATT	1260
Db		CAAGTCAGGAAGGTCTATGTGAGAAATATTTGTAAAGCTCTTTTGGATGTGCTTGGAATT	1260
Qу	1261	GAGGTAGATGCAGAGTACTTGTTGGGCCCACTTTATGCAGCTTTGAAAATGGAAAGTATG	1320
Db	1261	GAGGTAGATGCAGAGTACTTGTTGGGCCCACTTTATGCAGCTTTGAAAATGGAAAGTATG	1320
Qу	1321	GAAATCATTGAGGAGATTCAATGCCAAACTCAACAGGAAAACCTCAGCAGTAATAGTGAT	1380
Db	1321	GAAATCATTGAGGAGATTCAATGCCAAACTCAACAGGAAAACCTCAGCAGTAATAGTGAT	1380
Qу	1381	GGAATATCACCCAAAAGGCGTCGTCTCAGCTCGTCTCTAAACCCTTCTAAAAGAGCACCA	1440
Db	1381	GGAATATCACCCAAAAGGCGTCGTCTCAGCTCGTCTCTAAAACCCTTCTAAAAGAGCACCA	1440
Qу	1441	ÄAACAGACTGAGGAAATTAAACATGTGGACATGAACCAAAAGAGCATATTATGGAGTGCA	1500
Db	1441	AAACAGACTGAGGAAATTAAACATGTGGACATGAACCAAAAGAGCATATTATGGAGTGCA .	1500
Qу		CTGAAACAGAAAGCTGAATCCCTTCAGATTTCCCTTGAATACAGTGGCCTAAAGAATCCT	1560
Db			1560
QУ	•		1620
Db		${\tt GTTATTGAGATGTTAGAAGGAATTGCTGTTGTCTTACAACTGACTG$	1620
Qу		CATTGTTCTCATCAAAACATGAACTGCCGTACTTTCAAGGACTGTCAACATAAATCCAAG	
Db		CATTGTTCTCATCAAAACATGAACTGCCGTACTTTCAAGGACTGTCAACATAAATCCAAG	
Qу		AAGAAACCTTCTGTAGTGATAACTTGGATGTCATTGGATTTTTACACAAAAGTGCTTAAG	1740
Db			1740
δλ		AGCTGTAGAAGTTTGTTAGAATCTGTTCAGAAACTGGACCTGGAGGCAACCATTGATAAG	
Db		AGCTGTAGAAGTTTGTTAGAATCTGTTCAGAAACTTGGACCTGGAGGCAACCATTGATAAG	
δλ		#######################################	1860
Db			1860
Qу	1801	ATCCTGGAAGATTTATGTGGTATGCTCTCACTTCCATGGATTTATTCCCATTCTGATGAT	1920

Db	1861	${\tt ATCCTGGAAGATTTATGTGGTATGCTCTCACTTCCATGGATTTATTCCCATTCTGATGAT}$	1920
Qy	1921	GGCTGTTTAAAGTTGACCACATTTGCCGCTAATCTTCTAACATTAAGCTGTAGGATTTCA	1980
Db	1921	GGCTGTTTAAAGTTGACCACATTTGCCGCTAATCTTCTAACATTAAGCTGTAGGATTTCA	1980
Qγ .	1981	GATAGCTATTCACCACAGGCACAATCACGATGTGTGTTTCTTGACTCTGTTTCCAAGA	2040
Db	1981	GATAGCTATTCACCACAGGCACAATCACGATGTGTGTTTCTTGACTCTGTTTCCAAGA	2040
ДУ		AGAATAȚTCCTTGAGTGGAGAACAGCAGTTTACAACTGGGCCCTGCAGAGCTCCCATGAA	
Db		AGAATATTCCTTGAGTGGAGAACAGCAGTTTACAACTGGGCCCTGCAGAGCTCCCATGAA	
Qy		GTAATCCGGGCTAGTTGTGTTAGTGGATTTTTTATCTTATTGCAGCAGCAGAATTCTTGT	
Db		GTAATCCGGGCTAGTTGTTAGTGGATTTTTTATCTTATTGCAGCAGCAGAATTCTTGT	
Qy		AACAGAGTTCCCAAGATTCTTATAGATAAAGTCAAAGATGATTCTGACATTGTCAAGAAA	
Db		AACAGAGTTCCCAAGATTCTTATAGATAAAGTCAAAGATGATTCTGACATTGTCAAGAAA	
Qy Db		GAATTTGCTTCTATACTTGGTCAACTTGTCTGTACTCTTCACGGCATGTTTTATCTGACA	
		AGTTCTTTAACAGAACCTTTCTCTGAACACGGACATGTGGACCTCTTCTGTAGGAACTTG	
Qy Db		AGTTCTTTAACAGAACCTTTCTCTGAACACGGACATGTGGACCTCTTCTGTAGGAACTTG	
Qy		AAAGCCACTTCTCAACATGAATGTTCATCTTCTCAACTAAAAGGTTCTGTCTG	
Db		AAAGCCACTTCTCAACATGAATGTTCATCTTCTCAACTAAAAGCTTCTGTCTG	
Qy		TTCCTTTTCCTACTGAAAAAAAAAAATACCTAGTCCAGTAAAACTTGCTTTCATAGATAAT	
Db	2401		2460
Qy .	2461	CTACATCATCTTTGTAAGCATCTTGATTTTAGAGAAGATGAAACAGATGTAAAAGCAGTT	2520
Db	2461		2520
Qy	2521	$\tt CTTGGAACTTTATTAAATTTAATGGAAGATCCAGACAAAGATGTTAGAGTGGCTTTTAGT$	2580
Db	2521	CTTGGAACTTTATTAAATTTAATGGAAGATCCAGACAAAGATGTTAGAGTGGCTTTTAGT	2580
Qy	2581	${\tt GGAAATATCAAGCACATATTGGAATCCTTGGACTCTGAAGATGGATTTATAAAGGAGCTT}$	2640
Db	2581	GGAAATATCAAGCACATATTGGAATCCTTGGACTCTGAAGATGGATTTATAAAGGAGCTT	2640
Qу	2641	TTTGTCTTAAGAATGAAGGAAGCATATACACATGCCCAAATATCAAGAAATAATGAGCTG	2700
Db	2641	TTTGTCTTAAGAATGAAGGAAGCATATACACATGCCCAAATATCAAGAAATAATGAGCTG	2700
QУ	2701	AAGGATACCTTGATTCTTACAACAGGGGATATTGGAAGGGCCGCAAAAGGAGATTTGGTA	2760
Db		${\tt AAGGATACCTTGATTCTTACAACAGGGGGATATTGGAAGGGCCGCAAAAGGAGATTTGGTA}$	
Qy	2761	CCATTTGCACTCTTACACTTATTGCATTGTTTTGTTATCCAAGTCAGCATCTGTCTCTGGA	2820
Db	2761		2820
Qy .		GCAGCATACACAGAAATTAGAGCTCTGGTTGCAGCTAAAAGTGTTAAACTGCAAAGTTTT	2880
Db		GCAGCATACACAGAAATTAGAGCTCTGGTTGCAGCTAAAAGTGTTAAACTGCAAAGTTTT	2880
Qу		TTCAGCCAGTATAAGAAACCCATCTGTCAGTTTTTGGTAGAATCCCTTCACTCTAGTCAG	
Db		TTCAGCCAGTATAAGAAACCCATCTGTCAGTTTTTGGTAGAATCCCTTCACTCTAGTCAG	
Qy Db			3000
Qy		CACCAGAGAGAAATGGCTTTAAATACGTTGTCTGAAAATTGCCAACGTTTTCGACTTTCCT	
×1	2001		2000

Db .	3001	${\tt CACCAGAGAGAAATGGCTTTAAATACGTTGTCTGAAATTGCCAACGTTTTCGACTTTCCT}$	3060
Qу	3061	GATCTTAATCGTTTTCTTACTAGGACATTACAAGTTCTACTACCTGATCTTGCTGCCAAA	3120
Db	3061	GATCTTAATCGTTTTCTTACTAGGACATTACAAGTTCTACTACCTGATCTTGCTGCCAAA	3120
Qy	3121	GCAAGCCCTGCAGCTTCTGCTCTCATTCGAACTTTAGGAAAACAATTAAATGTCAATCGT	3180
Db	3121		3180
Qу	3181	AGAGAGATTTTAATAAACAACTTCAAATATATTTTTTCTCATTTGGTCTGTTCTTGTTCC	3240
Db	3181	AGAGAGATTTTAATAAACAACTTCAAATATATTTTTTTCTCATTTGGTCTGTTCTTGTTCC	3240
Qу	3241	AAAGATGAATTAGAACGTGCCCTTCATTATCTGAAGAATGAAACAGAAATTGAACTGGGG	3300
Db .	3241	AAAGATGAATTAGAACGTGCCCTTCATTATCTGAAGAATGAAACAGAAATTGAACTGGGG	3300
QУ	3301	AGCCTGTTGAGACAAGATTTCCAAGGATTGCATAATGAATTATTGCTGCGTATTGGAGAA	3360
Db	3301	AGCCTGTTGAGACAAGATTTCCAAGGATTGCATAATGAATTATTGCTGCGTATTGGAGAA	3360
Qу		CACTATCAACAGGTTTTTAATGGTTTGTCAATACTTGCCTCATTTGCATCCAGTGATGAT	
Db ·	3361	CACTATCAACAGGTTTTTAATGGTTTGTCAATACTTGCCTCATTTGCATCCAGTGATGAT	3420
QУ	3421	CCATATCAGGGCCCGAGAGATATCATATCACCTGAACTGATGGCTGATTATTTACAACCC	3480
Db	3421	· CCATATCAGGGCCCGAGAGATATCATATCACCTGAACTGATGGCTGATTATTTACAACCC	3480
Qу		AAATTGTTGGGCATTTTGGCTTTTTTTAACATGCAGTTACTGAGCTCTAGTGTTGGCATT	
Db		AAATTGTTĞGGCATTTTGGCTTTTTTTAACATGCAGTTACTGAGCTCTAGTGTTGGCATT	
QУ		GAAGATAAGAAAATGGCCTTGAACAGTTTGATGTCTTTGATGAAGTTAATGGGACCCAAA	
Db		GAAGATAAGAAAATGGCCTTGAACAGTTTGATGTCTTTGATGAAGTTAATGGGACCCAAA	
Qy Di-		CATGTCAGTTCTGTGAGGGTGAAGATGATGACCACACTGAGAACTGGCCTTCGATTCAAG	
Db		CATGTCAGTTCTGTGAGGGTGAAGATGATGACCACACTGAGAACTGGCCTTCGATTCAAG GATGATTTTCCTGAATTGTGTTGCAGAGCTTGGGACTGCTTTGTTCGCTGCCTGGATCAT	
Qy Db		GATGATTTTCCTGAATTGTGTTGCAGAGCTTGGGACTGCTTTGTTCGCTGCCTGGATCAT	
Qy		GCTTGTCTGGGCTCCCTTCTCAGTCATGTAATAGTAGCTTTGTTACCTCTTATACACATC	
Db		GCTTGTCTGGGCTCCCTTCTCAGTCATGTAATAGTAGCTTTGTTACCTCTTATACACATC	
Qy		CAGCCTAAAGAAACTGCAGCTATCTTCCACTACCTCATAATTGAAAACAGGGATGCTGTG	
Db			3840
Qу	3841	CAAGATTTTCTTCATGAAATATATTTTTTACCTGATCATCCAGAATTAAAAAAAGATAAAA	3900
Db	3841		3900
Qу	3901		3960
Db	3901		3960
Qy	3961	CAGCTCTCTATGAAGGCCATTCAACATGAAAATGTCGATGTTCGTATTCATGCTCTTACA	4020
Db	3961		4020
Qу	4021	${\tt AGCTTGAAGGAAACCTTGTATAAAAATCAGGAAAAACTGATAAAGTATGCAACAGACAG$	4080
Db	4021	AGCTTGAAGGAAACCTTGTATAAAAATCAGGAAAAACTGATAAAGTATGCAACAGACAG	4080
Qу	4081	GAAACAGTAGAACCTATTATCTCACAGTTGGTGACAGTGCTTTTGAAAGGTTGCCAAGAT	4140
Db	4081	GAAACAGTAGAACCTATTATCTCACAGTTGGTGACAGTGCTTTTGAAAGGTTGCCAAGAT	4140
QУ	4141	GCAAACTCTCAAGCTCGGTTGCTCTGTGGGGAATGTTTAGGGGAATTGGGGGCGATAGAT	4200

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Db		4141	${\tt GCAAACTCTCAAGCTCGGTTGCTCTGTGGGGAATGTTTAGGGGAATTGGGGGCGATAGAT}$	4200
Qу		4201	CCAGGTCGATTAGATTTCTCAACAACTGAAACTCAAGGAAAAGATTTTACATTTGTGACT	4260
Db		4201	CCAGGTCGATTAGATTTCTCAACAACTGAAACTCAAGGAAAAGATTTTACATTTGTGACT	4260
ДУ		4261	GGAGTAGAAGATTCAAGCTTTGCCTATGGATTATTGATGGAGCTAACAAGAGCTTACCTT	4320
Db		4261		4320
Qy		4321	GCGTATGCTGATAATAGCCGAGCTCAAGATTCAGCTGCCTATGCCATTCAGGAGTTGCTT	4380
Db		4321	GCGTATGCTGATAATAGCCGAGCTCAAGATTCAGCTGCCTATGCCATTCAGGAGTTGCTT	4380
Qу		4381	TCTATTTATGACTGTAGAGAGATGGAGACCAACGGCCCAGGTCACCAATTGTGGAGGAGA	4440
Db		4381	TCTATTTATGACTGTAGAGAGATGGAGACCAACGGCCCAGGTCACCAATTGTGGAGGAGA	4440
Qу		4441	TTTCCTGAGCATGTTCGGGAAATACTAGAACCTCATCTAAATACCAGATACAAGAGTTCT	4500
Db		4441	TTTCCTGAGCATGTTCGGGAAATACTAGAACCTCATCTAAATACCAGATACAAGAGTTCT	4500
Qу		4501	CAGAAGTCAACCGATTGGTCTGGAGTAAAGAAGCCAATTTACTTAAGTAAATTGGGTAGT	4560
Db		4501	CAGAAGTCAACCGATTGGTCTGGAGTAAAGAAGCCAATTTACTTAAGTAAATTGGGTAGT	4560
Qу		4561	AACTTTGCAGAATGGTCAGCATCTTGGGCAGGTTATCTTATTACAAAGGTTCGACATGAT	4620
Db		4561	${\tt AACTTTGCAGAATGGTCAGCATCTTGGGCAGGTTATCTTATTACAAAGGTTCGACATGAT}$	4620
Qу		4621	CTTGCCAGTAAAATTTTCACCTGCTGTAGCATTATGATGAAGCATGATTTCAAAGTGACC	4680
Db		4621	${\tt CTTGCCAGTAAAATTTTCACCTGCTGTAGCATTATGATGAAGCATGATTTCAAAGTGACC}.$	4680
Qу		4681	ATCTATCTTCCACATATTCTGGTGTATGTCTTACTGGGTTGTAATCAAGAAGATCAG	4740
ĎЬ		4681	ATCTATCTTCTCCACATATTCTGGTGTATGTCTTACTGGGTTGTAATCAAGAAGATCAG	4740
QУ		4741	CAGGAGGTTTATGCAGAAATTATGGCAGTTCTAAAGCATGACGATCAGCATAACAT	4800
Db		4741	CAGGAGGTTTATGCAGAAATTATGGCAGTTCTAAAGCATGACGATCAGCATAACATAAAT	4800
Qу		4801	ACCCAAGACATTGCATCTGATCTGTCAACTCAGTACACAGACTGTGTTCTCCATGCTT	4860
Db		4801	ACCCAAGACATTGCATCTGATCTGTTCAACTCAGTACACAGACTGTGTTCTCCATGCTT	4860
QУ		4861	GACCATCTCACACAGTGGGCAAGGCACAAATTTCAGGCACTGAAAGCTGAGAAATGTCCA	4920
Db		4861	GACCATCTCACACAGTGGGCAAGGCACAAATTTCAGGCACTGAAAGCTGAGAAATGTCCA	4920
.Qy		4921	CACAGCAAATCAAACAGAAATAAGGTAGACTCAATGGTATCTACTGTGGATTATGAAGAC	4980
Db		4921	CACAGCAAATCAĄACAGAAATAAGGTAGACTCAATGGTATCTACTGTGGATTATGAAGAC	4980
Qу		4981	TATCAGAGTGTAACCCGTTTTCTAGACCTCATACCCCAGGATACTCTGGCAGTAGCTTCC	5040
Db		4981	TATCAGAGTGTAACCCGTTTTCTAGACCTCATACCCCAGGATACTCTGGCAGTAGCTTCC	5040
Qу		5041	TTTCGCTCCAAAGCATACACACGAGCTGTAATGCACTTTGAATCATTTATTACAGAÃAAG	.5100
Db		5041	TTTCGCTCCAAAGCATACACACGAGCTGTAATGCACTTTGAATCATTTATTACAGAAAAG	5100
Qу			AAGCAAAATATTCAGGAACATCTTGGATTTTTACAGAAATTGTATGCTGCTATGCATGAA	
Db			AAGCAAAATATTCAGGAACATCTTGGATTTTTACAGAAATTGTATGCTGCTATGCATGAA	
Qу			CCTGATGGAGTGGCCGGAGTCAGTGCAATTAGAAAGGCAGACCATCTCTAAAAGAACAG	
Db			CCTGATGGAGTGGCCGGAGTCAGTGCAATTAGAAAGGCAGAACCATCTCTAAAAGAACAG	
Qу			ATCCTTGAACATGAAAGCCTTGGCTTGCTGAGGGATGCCACTGCTTGTTATGACAGGGCT	
Db			ATCCTTGAACATGAAAGCCTTGGCTTGCTGAGGGATGCCACTGCTTGTTATGACAGGGCT	
Qу		2781	ATTCAGCTAGAACCAGACCAGATCATTCATTATCATGGTGTAGTAAAGTCCATGTTAGGT	2340

Db	5281	ATTCAGCTAGAACCAGACCAGATCATTCATTATCATGGTGTAGTAAAGTCCATGTTAGGT	5340
Qу	5341	CTTGGTCAGCTGTCTACTGTTATCACTCAGGTGAATGGAGTGCATGCTAACAGGTCCGAG	5400
Db	5341	CTTGGTCAGCTGTCTACTGTTATCACTCAGGTGAATGGAGTGCATGCTAACAGGTCCGAG	5400
Qу	5401	TGGACAGATGAATTAAACACGTACAGAGTGGAAGCAGCTTGGAAATTGTCACAGTGGGAT	5460
Db	5401	TGGACAGATGAATTAAACACGTACAGAGTGGAAGCAGCTTGGAAATTGTCACAGTGGGAT	5460
Qy	5461	TTGGTGGAAAACTATTTGGCAGCAGATGGAAAATCTACAACATGGAGTGTCAGACTGGGA	5520
Db		TTGGTGGAAAACTATTTGGCAGCAGATGGAAAATCTACAACATGGAGTGTCAGACTGGGA	
QУ		CAGCTATTATTATCAGCCAAAAAAAGAGATATCACAGCTTTTTATGACTCACTGAAACTA	
Db		CAGCTATTATTATCAGCCAAAAAAAAAGAGATATCACAGCTTTTTATGACTCACTGAAACTA	
Qy Db		GTGAGAGCAGAACAAATTGTACCTCTTTCAGCTGCAAGCTTTGAAAGAGGGCTCCTACCAA	
Qy		CGAGGATATGAATATTGTGAGATTGCACATGTTATGTGAGTTGGAGCATAGCATCAAA	
Db			
QΥ ·	5701	CCACTTTTCCAGCATTCTCCAGGTGACAGTTCTCAAGAAGATTCTCTAAACTGGGTAGCT	5760
Db	5701	CACTTTTCCAGCATTCTCCAGGTGACAGTTCTCAAGAAGATTCTCTAAACTGGGTAGCT	5760
Qу	5761	CGACTAGAAATGACCCAGAATTCCTACAGAGCCAAGGAGCCTATCCTGGCTCTCCGGAGG	5820
Db	5761	CGACTAGAAATGACCCAGAATTCCTACAGAGCCAAGGAGCCTATCCTGGCTCTCCGGAGG	5820
Qy	5821	GCTTTACTAAGCCTCAACAAAAGACCAGATTACAATGAAATGGTTGGAGAATGCTGGCTG	5880
Db.	5821		5880
QУ	5881	CAGAGTGCCAGGGTAGCTAGAAAGGCTGGTCACCACAGACAG	5940
Db		CAGAGTGCCAGGGTAGCTAGAAAGGCTGGTCACCACCAGACAGCCTACAATGCTCTCCTT	5940
QУ		AATGCAĞGGGAATCACGACTCGCTGAACTGTACGTGGAAAGGGCAAAGTGGCTCTGGTCC	
Db		AATGCAGGGGAATCACGACTCGCTGAACTGTACGTGGAAAGGGCAAAGTGGCTCTGGTCC	6000
Qy Db		AAGGGTGATGTTCACCAGGCACTAATTGTTCTTCAAAAAGGTGTTGAATTATGTTTTCCT	6060
Qy		GAAAATGAAACCCACCTGAGGGTAAGAACATGTTAATCCATGGTCGAGCTATGCTACTA	6060
Db		GAAAAT GAAACCCCACCT GAGGGTAAGAACATGTTAATCCATGGTCGAGCTATGCTACTA	
Qy .	6121	GTGGGCCGATTTATGGAAGAAACAGCTAACTTTGAAAGCAATGCAATTATGAAAAAAATAT	6180
Db	6121		6180
QУ	6181	AAGGATGTGACCGCGTGCCTGCCAGAATGGGAGGATGGGCATTTTTACCTTGCCAAGTAC	6240
Db	6181	AAGGATGTGACCGCGTGCCTGCCAGAATGGGAGGATGGGCATTTTTACCTTGCCAAGTAC	6240
Ωу	6241	TATGACAAATTGATGCCCATGGTCACAGACAACAAAATGGAAAAGCAAGGTGATCTCATC	6300
Db	6241	TATGACAAATTGATGCCCATGGTCACAGACAACAAATGGAAAAGCAAGGTGATCTCATC	6300
Qу	6301	CGGTATATAGTTCTTCATTTTGGCAGATCTCTACAATATGGAAATCAGTTCATATATCAG	6360
Db	6301	CGGTATATAGTTCTTCATTTTGGCAGATCTCTACAATATGGAAATCAGTTCATATATCAG	6360
Qу		TCAATGCCACGAATGTTAACTCTATGGCTTGATTATGGTACAAAGGCATATGAATGGGAA	
Db		TCAATGCCACGAATGTTAACTCTATGGCTTGATTATGGTACAAAGGCATATGAATGGGAA	
Ĉλ .	6421	AAAGCTGGCCGCTCCGATCGTGTACAAATGAGGAATGATTTGGGTAAAATAAACAAGGTT	6480

Db	6421	${\tt AAAGCTGGCCGCTCCGATCGTGTACAAATGAGGAATGATTTGGGTAAAATAAACAAGGTT}$	6480
Qy	6481	ATCACAGAGCATACAAACTATTTAGCTCCATATCAATTTTTGACTGCTTTTTCACAATTG	6540
Db	6481	ATCACAGAGCATACAAACTATTTAGCTCCATATCAATTTTTGACTGCTTTTTCACAATTG	6540
Qy	6541	ATCTCTCGAATTTGTCATTCTCACGATGAAGTTTTTGTTGTTCTTGATGGAAATAATAGCC	
Db	6541	ATCTCTCGAATTTGTCATTCTCACGATGAAGTTTTTGTTGTTGTTGATGGAAATAATAGCC	
Qy	6601	AAAGTATTTCTAGCCTATCCTCAACAAGCAATGTGGATGATGACAGCTGTGTCAAAGTCA	6660
Db	6601	AAAGTATTTCTAGCCTATCCTCAACAAGCAATGTGGATGATGACAGCTGTGTCAAAGTCA	6660
Qy	6661	TCTTATCCCATGCGTGTGAACAGATGCAAGGAAATCCTCAATAAAGCTATTCATATGAAA	6720
Db		TCTTATCCCATGCGTGTGAACAGATGCAAGGAAATCCTCAATAAAGCTATTCATATGAAA	
Qγ		AAATCCTTAGAGAAGTTTGTTGGAGATGCAACTCGCCTAACAGATAAGCTTCTAGAATTG	
Db		AAATCCTTAGAGÄAGTTTGTTGGAGATGCAACTCGCCTAACAGATAAGCTTCTAGAATTG	
Qу		TGCAATAAACCGGTTGATGGAAGTAGTTCCACATTAAGCATGAGCACTCATTTTAAAATG	
Db		TGCAATAAACCGGTTGATGGAAGTAGTTCCACATTAAGCATGAGCACTCATTTTAAAATG	
Qγ Db ·		CTTAAAAAGCTGGTAGAAGAAGCAACATTTAGTGAAATCCTCATTCCTCTACAATCAGTC	
Qy		ATGATACCTACACTTCCATCAATTCTGGGTACCCATGCTAACCATGCTAGCCATGAACCA	
V-		ATGATACCTACACTTCCATCAATTCTGGGTACCCATGCTAACCATGCTAGCCATGAACCA	
Qy		TTTCCTGGACATTGGGCCTATATTGCAGGGTTTGATGATATGGTGGAAATTCTTGCTTCT	
Db		TTTCCTGGACATTGGGCCTATATTGCAGGGTTTGATGATATGGTGGAAATTCTTGCTTCT	7020
Qу	7021	CTTCAGAAACCAAAGAAGATTTCTTTAAAAGGCTCAGATGGAAAGTTCTACATCATGATG	7080
Db	7021		7080
Qy	7081	TGTAAGCCAAAAGATGACCTGAGAAAGGATTGTAGACTAATGGAATTCAATTCCTTGATT	7140
Db	7081	TGTAAGCCAAAAGATGACCTGAGAAAGGATTGTAGACTAATGGAATTCAATTCCTTGATT	7140
Qy	7141	AATAAGTGCTTAAGAAAAGATGCAGAGTCTCGTAGAAGAGAACTTCATATTCGAACATAT	7200
Db	7141		7200
Qу	7201	GCAGTTATTCCACTAAATGATGATGTGGGATTATTGAATGGGTGAACAACACTGCTGGT	7260
Db	7201	GCAGTTATTCCACTAAATGATGAATGTGGGATTATTGAATGGGTGAACAACACTGCTGGT	7260
QУ	7261	TTGAGACCTATTCTGACCAAACTATATAAAGAAAAGGGAGTGTATATGACAGGAAAAGAA	7320
Db	7261	TTGAGACCTATTCTGACCAAACTATATAAAGAAAAGGGAGTGTATATGACAGGAAAAGAA	7320
Qy ,	7321	CTTCGCCAGTGTATGCTACCAAAGTCAGCAGCTTTATCTGAAAAACTCAAAGTATTCCGA	7380
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Qу		GAATTTCTCCTGCCCAGGCATCCTCCTATTTTTCATGAGTGGTTTCTGAGAACATTCCCT	
Db		GAATTTCTCCTGCCCAGGCATCCTCCTATTTTTCATGAGTGGTTTCTGAGAACATTCCCT	
QУ		GATCCTACATCATGGTACAGTAGTAGATCAGCTTACTGCCGTTCCACTGCAGTAATGTCA	
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ДУ		ATGGTTGGTTATATTCTGGGGCTTGGAGACCGTCATGGTGAAAATATTCTCTTTGATTCT	7560
Qy		TTGACTGGTGAATGCGTACATGTAGATTTCAATTGTCTTTTCAATAAGGGAGAAACCTTT	7620

•				
	Db	7561	${\tt TTGACTGGTGAATGCGTACATGTAGATTTCAATTGTCTTTTCAATAAGGGAGAAACCTTT}$	7620
	Qу	7621	GAAGTTCCAGAAATTGTGCCATTTCGCCTGACTCATAATATGGTTAATGGAATGGGTCCT	7680
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	Qу	7681	$\tt ATGGGAACAGAGGGTCTTTTTCGAAGAGCATGTGAAGTTACAATGAGGCTGATGCGTGAT$	7740
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	ΩУ	7981	GAAGCTACTGATGAAAACTTACTATGCCAGATGTATCTTGGTTGG	8040
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	Qy	8041	AATGAAATTATGTAAAAGAATATGTTAATAATCTAAAAGTAATGCATTTGGTATGAATCT	8100
	Db	8041		8100
	Qγ	8101	GTGGTTGTATCTGTTCAATTCTAAAGTACAACATAAATTTACGTTCTCAGCAACTGTTAT	8160
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	QУ	8161	TTCTCTCTGATCATTAATTATATGTAAAATAATATACATTCAGTTATTAAGAAATAAACT	8220
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	Qy	8221	GCTTTCTTAATAAAAAAAAAAAAAAAAAAAAAAAAAAAA	
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# Exhibito

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US-10-388-360-295
; Sequence 295, Application US/10388360
 Patent No. 7081340
 GENERAL INFORMATION:
  APPLICANT: GENOMIC HEALTH
 APPLICANT: Baker, Joffre B.
  APPLICANT: Cronin, Maureen T.
  APPLICANT:
          Kiefer, Michael C.
  APPLICANT: Shak, Steve
  APPLICANT: Walker, Michael Graham
  TITLE OF INVENTION: GENE EXPRESSION PROFILING IN BIOPSIED TUMOR TISSUES
  FILE REFERENCE: 39740-0001US
  CURRENT APPLICATION NUMBER: US/10/388,360
  CURRENT FILING DATE:
                 2003-03-12
  PRIOR APPLICATION NUMBER: US 60/412,049
  PRIOR FILING DATE: 2002-09-18
  PRIOR APPLICATION NUMBER: US 60/364,890
  PRIOR FILING DATE: 2002-03-13
  NUMBER OF SEQ ID NOS: 384
  SOFTWARE: FastSEQ for Windows Version 4.0
 SEQ ID NO 295
  LENGTH: 2042
  TYPE: DNA
   ORGANISM: Homo sapiens
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 Matches 2042; Conservative
                       0; Mismatches
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Qy
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          241 ATAGAGTAACTGAAGAAGCAGTCGCAGTGAAGATTGTAGATATGAAGCGTGCCGTAGACT 300
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          Db
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Qγ
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Db	781	GGGACCAACCCAGTGACAGCTGTCAGGAGTATTCTGACTGGAAAGAAA	840
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Qу	1021	GTGGATTTCTAAGCACATTCAATCCAATTTGGACTTCTCCAGTAAACAGTGCTTCTA	1080
Db	1021	GTGGATTTTCTAAGCACATTCAATCCAATTTGGACTTCTCCCAGTAAACAGTGCTTCTA	1080
Qу	1081	GTGAAGAAATGTGAAGTACTCCAGTTCTCAGCCAGAACCCCGCACAGGTCTTTCCTTAT	1140
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Qy 		GGGATACCAGCCCTCATACATTGATAAATTGGTACAAGGGATCAGCTTTTCCCAGCCCA	
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Qу Db	•	CATGTCCTGATCATATGCTTTTGAATAGTCAGTTACTTGGCACCCCAGGATCCTCACAGA	
ΩУ		CATGTCCTGATCATATGCTTTTGAATAGTCAGTTACTTGGCACCCCAGGATCCTCACAGA  ACCCCTGGCAGCGGTTGGTCAAAAGAATGACACGATTCTTTACCAAATTGGATGCAGACA	
DΡ		ACCCCTGGCAGCGGTTGGTCAAAAGAATGACACGATTCTTTACCAAATTGGATGCAGACA	
Qy	•	AATCTTATCAATGCCTGAAAGAGACTTGTGAGAAGTTGGGCTATCAATGGAAGAAAAGTT	
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Qу	1381	GTATGAATCAGGTTACTATATCAACAACTGATAGGAGAAACAATAAACTCATTTTCAAAG	1440
Db	1381		1440
Qу	1441	TGAATTTGTTAGAAATGGATGATAAAATATTGGTTGACTTCCGGCTTTCTAAGGGTGATG	1500
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Qу	1561	GCCAGAAGGTTTGGCTTCCTGCCACATGATCGGACCATCGGCTCTGGGGAATCCTGGTGA	1620
Db	1561	GCCAGAAGGTTTGGCTTCCTGCCACATGATCGGACCATCGGCTCTGGGGAATCCTGGTGA	1620
Qу	1621	ATATAGTGCTGCTATGTTGACATTATTCTTCCTAGAGAAGATTATCCTGTCCTGCAAACT	1680
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Qу		GCAAATAGTAGTTCCTGAAGTGTTCACTTCCCTGTTTATCCAAACATCTTCCAATTTATT	
Db		GCAAATAGTAGTTCCTGAAGTGTTCACTTCCCTGTTTATCCAAACATCTTCCAATTTATT	
ДУ		TTGTTTGTTCGGCATACAAATAATACCTATATCTTAATTGTAAGCAAAACTTTGGGGAAA	
Db		TTGTTTGTTCGGCATACAAATAATACCTATATCTTAATTGTAAGCAAAACTTTGGGGAAA	
Qу	1801	GGATGAATAGAATTCATTTGATATTTCTTCATGTGTTTTAGTATCTGAATTTGAAACT	1860

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Qу
    Db
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Qу
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